REMARKS

Applicant respectfully requests that the foregoing amendments be made prior to examination of the present application.

Claims 1-4 and 10 are currently being amended.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

After amending the claims as set forth above, claims 1-23 are pending in this application. It is noted that the Office action mailed 23 July 2004 indicates that claims 1-22 are pending, but the Office action mailed 21 April 2004 and applicants' records list claims 1-23 as pending. Thus, applicants believe that claims 1-23 are pending, and the listing of pending claims listed in the July 23rd Office action to be in error. If this is incorrect, applicants respectfully request the examiner's comments. Claims 1-6, 8, 10, 11, and 15 are now pending in this application, and claims 7, 9, 12-14, and 16-23 are withdrawn.[1]

Election/Restrictions

The examiner has made the restriction requirement final. Specifically, the examiner has agreed to examine claims 1, 2, 15 with claims 3-6, 8, and 10-11 and withdrawn claims 7, 9, 12-14, and 16-22 from consideration. Applicants respectfully traverse.

Applicants appreciate the examiners agreement that claims 1, 2, 15 should be examined with claims 3-6, 8, and 10-11. However, applicants traverse the remaining restriction requirement for reasons already of record.

[1] Applicants assume that claim 23 is pending and withdrawn further to the previous explanation.

Specification – Objection to Title

The examiner has objected to the title of the invention, because it is argued to be non-descriptive. Applicants respectfully disagree.

A "title should be brief but technically accurate and descriptive..." MPEP § 606. The present title is both brief and technically accurate. The six word title, "Extracellular Matrix And Adhesion-Associated Proteins," accurately describes the subject matter of the invention. The claimed subject matter covers extracellular matrix and adhesion-related polypeptides, the polynucleotides encoding such polypeptides, and related subject matter, such as vectors, antibodies, and agonists. Accordingly, the current title is both brief and technically accurate and should not be amended. The title suggested by the examiner may also be brief and technically accurate, but it should not replace the current title that already meets the guidelines set forth in MPEP § 609.

Claim Objections

Claim 3 is objected to, because the examiner argues that the claim is an improper dependent for failing to further limit the subject matter of a previous claim. Claim 3 has been rewritten in independent form. Thus, applicants respectfully request the objection be withdrawn.

Claim Rejections – 35 U.S.C. § 101 – Utility

Claims 1-6, 8, 10-11, and 15 are rejected by the examiner under 35 U.S.C. § 101 as lacking patentable utility. The examiner asserts that the specification does not support credible, substantial, or specific utility. Applicants respectfully disagree with the examiner's findings and respectfully request reconsideration and withdrawal of the rejection.

MPEP § 2107(II) states that "an applicant need only provide one credible assertion of specific and substantial utility for each claimed invention." Additionally, an applicant needs to "establish a probative relation between the submitted evidence and the originally disclosed properties of the claimed invention." On the basis of the above recited MPEP sections, the

original specification and the attached publication, applicants argue that the subject matter of the present application possesses specific and substantial utility as required under 35 U.S.C. § 101.

First, the original specification broadly identifies the utility of the invention on page 25 reciting its use for diagnosis, treatment, or prevention of cell proliferative, immune, reproductive, neuronal, and genetic disorders. The specification more specifically recites utility for SEQ ID NOS: 9 and 34 in Table 3. The table shows that SEQ ID NO: 34 is associated with cancer, inflammation, and cell proliferation. The specification includes extensive teachings of the different ways therapeutics and diagnostics. *See* Spec. at 35-50. Applicants a references supporting this utility.

Jang et al. *A Novel Leucine-Rich Repoeat Protein (LRR-1): Potential Involvement in 4-1BB-mediated Signal Transduction*, MOL. CELLS 12(3):304-12 (2001) (Exhibit A), discloses a peptide, LRR-1, with 100% sequence similarity with SEQ ID NO: 9. This peptide is shown to associate with 4-1BB. *See* Jang at 305. 4-1BB is a member of the tumor necrosis factor receptor (TNFR) superfamily. *See* Jang at Abstract. Interactions of 4-1BB with its ligand increase IL-2 production and proliferation and survival of T cells. *See* Jang at 304. Thus, this teaching supports the specifications teaching of diagnostics and treatments for immune conditions. LRR-1 is also shown to down-regulate 4-1BB-mediated NF-$\kappa\beta$ and JNK1 activation. *See* Jang at 305. NF-$\kappa\beta$ is know to be associated with cancer. Thus, this teaching supports the specifications teaching of diagnostics and treatments for cancer. In summary, this reference wholly supports the specific utilities for SEQ ID NO: 34 disclosed in Table 3 of the specification.

In light of the above identified uses for the claimed protein sequence compositions, applicants argue that the subject matter of the claimed invention discloses at least "one credible assertion of specific and substantial utility" and thus, satisfies the requirements of 35 U.S.C. §101. Therefore, applicants argue that this rejection should be withdrawn and the present claims allowed.

Claim Rejections 35 U.S.C. § 112, ¶ 1 – Written Description

Claims 1-6, 8, 10-11, and 15 are rejected by the examiner under 35 U.S.C. § 112, ¶ 1, because the examiner states that the claimed invention is supported by neither a substantially asserted utility nor a well established utility. As set forth above, applicants assert that the present application provides a specific and substantial as well as a well-established utility for the claimed invention. Thus, applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 1-3, 5-6, 8, 10-11, and 15 are rejected by the examiner under 35 U.S.C. § 112, ¶ 1 as containing subject matter which was not described in the specification in such a way as to reasonable convey to one skilled in the relevant art that the inventors, at the time of filing, had possession of the claimed invention. Applicants respectfully disagree.

Claim 1 and 10 are rejected based on the recitation of "naturally occurring." As amended, neither claim 1(b) nor 10(b) recite "naturally occurring." Thus, the written description rejections based on these terms is rendered moot and should be withdrawn.

Claim 11 is rejected based on the recitation of "comprising at least 60 contiguous nucleotides." The examiner states that "[s]ince the disclosure fails to describe the common attributes or characteristics that identify member of the genus, and because the genus is highly variant, nucleic acid molecules comprising at least 60 contiguous nucleotides of SEQ ID NO:34 alone are insufficient to describe the genus."

However, the specification does describe common attributes and characteristics that identify members of the genus. For example, Table 2 shows structural features of the polypeptide encoded by SEQ ID NO: 34, including potential motifs, homologous sequences, and methods, algorithms, and databases used for the analysis of EXMAD. This information includes "signature sequence" information which shows that SEQ ID NO: 9, the polypeptide encoded by SEQ ID NO: 34, has a specifically defined signal peptide region and three leucine-rich repeats (LRR). The structure and function of leucine-rich repeats are discussed extensively on pages 6 to 7 of the specification. Specifically, LRR are known to be involved in protein-protein interactions, such as signal transduction and cellular adhesion. This

information provides common attributes and characteristics for identifying members of the genus. In light of the common attributes and characteristics contained in the specification, applicants argue that the written description rejection should be withdrawn and the present claims allowed.

Claim Rejections 35 U.S.C. § 112, ¶ 1 – Enablement

Claims 1-6, 8, 10-11, and 15 are rejected by the examiner under 35 U.S.C. § 112, ¶ 1, because the examiner states that the claimed invention is supported by neither a substantially asserted utility or a well established utility. As set forth above, applicants assert that the present application provides a specific and substantial as well as a well-established utility for the claimed invention. Thus, applicants respectfully request reconsideration and withdrawal of the rejection.

Claim 6 is rejected under 35 U.S.C. § 112, ¶ 1, because the specification, while being enabling for a host cell in culture comprising a polynucleotide with the sequence as set forth in SEQ ID NO: 34, is argued as not reasonably providing enablement for *in vivo* transfection. Applicant respectfully disagrees. However, to expedite prosecution applicants have amended claim 6 to include "isolated" as suggested by the examiner.

Claim 11 is rejected under 35 U.S.C. § 112, ¶ 1, because the specification, while being enabling for a polynucleotide comprising SEQ ID NO: 34, is argued as not reasonably providing enablement for a polynucleotide comprising at least 60 nucleotides of SEQ ID NO: 11. Specifically, the examiner states that the claimed sequence lacks sufficient structural and functional description necessary for enablement. The examiner also states that the specification fails to teach methods of making the polynucleotides comprising at least 60 nucleotides. Applicants respectfully disagree.

The examiner states that the issue involves the breadth of the claims in light of the predictability of the art, the skill level of the artisan, the guidance in the specification and the prior art of record. As an initial matter, the skill in the art is high. Skilled artisans in the field typically have a doctoral level of education along with experience. The predictability of the art is at least moderate, if not high. The ability to obtain and purify polynucleotides is a

routine laboratory procedure. *See, e.g.,* spec. at 27-29. The ability to manipulate polynucleotide libraries to obtain new polynucleotides is also routine. The specification gives extensive guidance on the structure and function of the claimed polynucleotides as discussed above in the written description section. While the breadth of the claim potentially covers a large number of polynucleotides, this alone is not sufficient to render the experimentation undue given the factors suggesting enablement.

Claims 1, 3-6, 8, 10-11, and 15 are rejected under 35 U.S.C. § 112, ¶ 1, because the specification, while being enabling for an isolated polynucleotide encoding SEQ ID NO: 9, is argued as not reasonably providing enablement for an isolated polynucleotide "'...having at least 90% identity to SEQ ID NO:34' or an isolated polypeptide '...having at least 90% identity to SEQ ID NO:9'." Applicants respectfully disagree.

As amended, claims 1 and 10 now require at least 95% sequence identity. Support for this amendment can be found on page 26, lines 26-29, for example. Thus, the breadth of the claims is narrow. As noted above, one of ordinary skill in the art has a level of skill typically consisting of a doctoral education and some practical experience. Thus, the skill in the art is very high. Moreover, the specification provides extensive guidance. For example, Table 2 describes potential phosphorylation and glycosylation sites, homologous sequences, and features of SEQ ID NO: 9, such as leucine-rich repeats (LRR). The specification discloses structural and functional characteristics of LRR. Table 3 shows the tissue-specificity and diseases, disorders, and conditions associated with the nucleotides encoding EXMAD, such as SEQ ID NO: 34. Methods of producing EXMAD, such as SEQ ID NO: 9, and methods of screening the peptides for biological activity in physiological systems are also provided. *See e.g.*, spec at 50-60. The specification also provides guidance on how to obtain polynucleotides encoding for extended EXMAD sequences. See Spec. at 28:9-29. Thus, the specification provides extensive guidance to allow one of ordinary skill in the art to recognize possession and obtain the narrow specific polypeptides and polynucleotides claimed and sequences at least 95% similar. Thus, applicants believe the *In re Wands* factors show that undue experimentation is not required to practice the invention as claimed. Applicants respectfully request the rejection be reconsidered and withdrawn.

Claim Rejections 35 U.S.C. § 112, ¶ 2

Claims 1-6, 8, 10-11, and 15 are rejected under 35 U.S.C. §112, ¶ 2 as being indefinite for failing to particularly point out and distinctly claim the subject matter considered the invention. Applicants respectfully disagree.

Claims 1, 2, 4, and 10 were rejected as reciting non-elected matter These claims have been amended to recite only the elected subject matter. Thus, the objections to the claims should be withdrawn.

Claims 1, 10 are rejected because of the recitation of the term "naturally occurring." Applicants respectfully disagree that the term "naturally occurring" renders claims 1 and 10 indefinite . However, to expedite prosecution applicants have amended claims 1 and 10 to remove the phrase "naturally occurring."

Claims 1, 10 are rejected because of the recitation of the term "immunogenic fragment." Applicants respectfully disagree with the examiner's objection to the term "immunogenic fragment." First, applicants note that claim 10 does not recite "immunogenic fragment" and that term is only recited in claim 1. Thus, the rejection of claim 10 on this basis is improper. Applicants also respectfully disagree with the rejection of claim 1 based on the recitation of "immunogenic fragment." However, to expedite prosecution applicants have amended claims 1 to remove claim 1(d) reciting the term "immunogenic fragment."

Claims 1 is rejected because of the recitation of the term "biologically active." Applicants respectfully disagree that the term "biologically active" renders claim 1 vague and indefinite. However, to expedite prosecution applicants have amended claim 1 to remove claim 1(c) containing the term "biologically active."

Claims 3, 5-6, 8, 11, 15 are rejected as vague and indefinite insofar as they depend on the above rejected claims. The amendments and remarks of record should make these rejections moot. Thus, applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, ¶ 2.

Claim Rejections 35 U.S.C. § 102

Claims 1-3, 5-6, 8, 10-11, and 15 are rejected by the examiner under 35 U.S.C. § 102 as being anticipated by Ntwasa et al (1994). The examiner argues that because Ntwasa et al. discloses a cDNA encoding the LRR47 protein, which was cloned and expressed, the disclosure teaches a "biologically active fragment" of the claimed polypeptides.

Claim 1 as amended no longer recites "biologically active fragment." Thus, the rejection should be withdrawn.

CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date 10/25/04

By _____

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